Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 13:40:24 ON 02 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:     1 FEB 2002  HIGHEST RN 389104-08-9
DICTIONARY FILE UPDATES:    1 FEB 2002  HIGHEST RN 389104-08-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02.  Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved.  Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies.  Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=> d ide can tot 147

L47  ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2002 ACS
RN   329967-85-3  REGISTRY
CN   Synthetase, prostaglandin endoperoxide, 1 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Arachidonate cyclooxygenase 1
CN   COX-1
CN   Cyclooxygenase 1
CN   Prostaglandin endoperoxide synthetase 1
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             211 REFERENCES IN FILE CA (1967 TO DATE)
             213 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:85672

REFERENCE   2:  136:80201

REFERENCE   3:  136:79359

REFERENCE   4:  136:68442

REFERENCE   5:  136:65550

REFERENCE   6:  136:64576
```

REFERENCE 7: 136:63779

REFERENCE 8: 136:63770

REFERENCE 9: 136:49587

REFERENCE 10: 136:49576

L47 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2002 ACS
RN **329900-75-6** REGISTRY
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase 2
CN COX 2
CN **Cyclooxygenase 2**
CN Prostaglandin endoperoxide synthase-2
CN Prostaglandin endoperoxide synthetase 2
CN Prostaglandin G/H synthase-2
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
732 REFERENCES IN FILE CA (1967 TO DATE)
748 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:90972

REFERENCE 2: 136:85758

REFERENCE 3: 136:84626

REFERENCE 4: 136:84018

REFERENCE 5: 136:83819

REFERENCE 6: 136:83720

REFERENCE 7: 136:83448

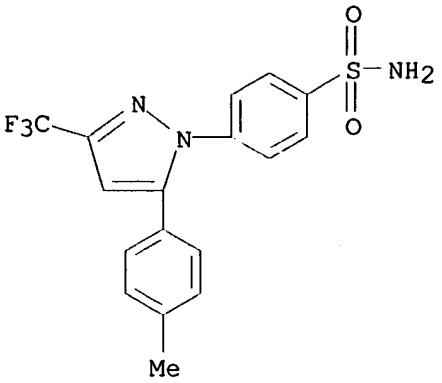
REFERENCE 8: 136:83390

REFERENCE 9: 136:80302

REFERENCE 10: 136:80290

L47 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2002 ACS
RN **169590-42-5** REGISTRY
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Celebrex
CN **Celecoxib**
CN Celocoxib
CN SC 58635
CN YM 177
FS 3D CONCORD
DR 184007-95-2, 194044-54-7
MF C17 H14 F3 N3 O2 S
CI COM
SR US Adopted Names Council
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA,

MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

271 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
272 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:90972

REFERENCE 2: 136:79446

REFERENCE 3: 136:69810

REFERENCE 4: 136:63539

REFERENCE 5: 136:63482

REFERENCE 6: 136:63449

REFERENCE 7: 136:58732

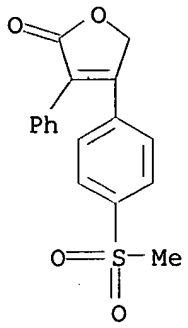
REFERENCE 8: 136:50368

REFERENCE 9: 136:48558

REFERENCE 10: 136:48407

L47 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2002 ACS
RN **162011-90-7** REGISTRY
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-Phenyl-4-[4-(Methylsulfonyl)phenyl]-2(5H)-furanone
CN MK 0966
CN MK 966
CN **Rofecoxib**
CN Vioxx
FS 3D CONCORD
DR 186912-82-3
MF C17 H14 O4 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA,

CAPLUS, CASREACT, CBNB, CEN, CIN, CSCHEM, DIOGENES, DRUGNL, DRUGPAT, DRUGUPDATES, EMBASE, IPA, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

194 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
196 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:90972

REFERENCE 2: 136:80195

REFERENCE 3: 136:79446

REFERENCE 4: 136:79147

REFERENCE 5: 136:64005

REFERENCE 6: 136:63602

REFERENCE 7: 136:63482

REFERENCE 8: 136:63449

REFERENCE 9: 136:50368

REFERENCE 10: 136:48173

L47 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2002 ACS
RN **39391-18-9** REGISTRY
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Arachidonate cyclooxygenase
CN Arachidonic acid cyclooxygenase
CN Arachidonic cyclooxygenase
CN **Cyclooxygenase**
CN E.C. 1.14.99.1
CN Fatty acid cyclooxygenase
CN Gene TIS10 proteïns
CN Peroxidase, prostaglandin hydroperoxide
CN PG synthetase
CN PGG/H synthase
CN PGG2 peroxidase
CN PGH synthase
CN PGH2 synthase

CN PGH2 synthetase
CN PGI2 cyclooxygenase
CN Prostaglandin cyclooxygenase
CN Prostaglandin endoperoxide G/H synthase
CN Prostaglandin endoperoxide H synthase
CN Prostaglandin endoperoxide synthase
CN Prostaglandin endoperoxide synthetase
CN Prostaglandin G/H synthase
CN Prostaglandin G2 peroxidase
CN Prostaglandin G2/H2 synthase
CN Prostaglandin H synthase
CN Prostaglandin H synthetase
CN Prostaglandin H2 synthase
CN Prostaglandin H2 synthetase
CN Prostaglandin hydroperoxidase
CN Prostaglandin hydroperoxide peroxidase
CN Prostaglandin peroxidase
CN Proteins, specific or class, gene TIS10
CN TXA2 cyclooxygenase
DR 59763-19-8, 64427-82-3, 69913-02-6
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, EMBASE, NIOSHTIC, PROMT, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7177 REFERENCES IN FILE CA (1967 TO DATE)
73 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7161 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:84634

REFERENCE 2: 136:84444

REFERENCE 3: 136:84089

REFERENCE 4: 136:80200

REFERENCE 5: 136:79132

REFERENCE 6: 136:67410

REFERENCE 7: 136:67126

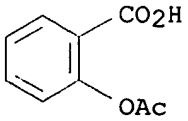
REFERENCE 8: 136:66317

REFERENCE 9: 136:65408

REFERENCE 10: 136:64557

L47 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2002 ACS
RN **50-78-2** REGISTRY
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-(Acetyloxy)benzoic acid
CN 2-Acetoxybenzoic acid
CN 2-Carboxyphenyl acetate
CN A.S.A. Empirin
CN AC 5230
CN Acenterine
CN Acesal
CN Acesan
CN Acetard
CN Aceticyl
CN Acetilum acidulatum

CN Acetisal
CN Acetol
CN Acetophen
CN Acetosal
CN Acetosalic acid
CN Acetosalin
CN Acetylin
CN Acetylsal
CN Acetylsalicylic acid
CN Acetysal
CN Acidum acetylsalicylicum
CN Acisal
CN Acylpyrin
CN ASA
CN Asagran
CN **Aspirin**
CN Aspirin Protect 100
CN Aspirin Protect 300
CN Aspirina 03
CN Aspro
CN Aspro Clear
CN Aspropharm
CN Asteric
CN Benaspir
CN Bialpirina
CN Caprin
CN Colfarit
CN Dolean pH 8
CN Duramax
CN ECM
CN Ecotrin
CN Empirin
CN Endosprin
CN Endydol
CN Enterosarine
CN Entrophen
CN Globentyl
CN Globoid
CN Helicon
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11126-35-5, 11126-37-7, 98201-60-6, 2349-94-2, 26914-13-6
MF C9 H8 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

```
        13929 REFERENCES IN FILE CA (1967 TO DATE)
          274 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
        13946 REFERENCES IN FILE CAPLUS (1967 TO DATE)
            1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE   1:  136:92324

REFERENCE   2:  136:90976

REFERENCE   3:  136:90966

REFERENCE   4:  136:90964

REFERENCE   5:  136:90959

REFERENCE   6:  136:90958

REFERENCE   7:  136:90827

REFERENCE   8:  136:87682

REFERENCE   9:  136:85672

REFERENCE  10:  136:85039


=> d his

     (FILE 'HOME' ENTERED AT 12:35:38 ON 02 FEB 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 12:37:00 ON 02 FEB 2002
L1             1 S ASPIRIN/CN
L2           482 S 50-78-2/CRN
L3             2 S (CELECOXIB OR ROFECOXIB)/CN
L4            10 S (169590-42-5 OR 162011-90-7)/CRN
L5             0 S L2 AND L4
               E CYCLOOXYGENASE/CN
L6             3 S E3,E6,E7

     FILE 'HCAPLUS' ENTERED AT 12:39:32 ON 02 FEB 2002
L7           448 S CELEBREX OR CELECOXIB OR CELOCOXIB OR YM177 OR YM 177 OR SC58
L8          9063 S L6
               E COX
L9           429 S E5
L10         1257 S E52
L11         3342 S COX()(2 OR 1)
L12        15098 S CYCLOOXYGENASE
L13         7592 S CYCLOOXYGENASE(L)2
L14         7109 S CYCLOOXYGENASE(L)1
L15         1073 S PROSTAGLANDIN(L)ENDOPEROXID?(L)(SYNTHETASE OR SYNTHASE)
L16        17880 S L8-L15
L17        14014 S L1
L18         1062 S L2
L19        15320 S ASPIRIN
L20         8244 S (ACETYLSALICYLIC OR ACETYL SALICYLIC)()ACID OR ACETOL
L21         1434 S (ACETOXYBENZOIC OR ACETOXY BENZOIC)()ACID
L22        25229 S L17-L21
L23         2134 S L16 AND L22
               E FLAVANOID/CT
               E E7+ALL
L24            4 S E1
               E E2+ALL
L25        32506 S E4+NT
L26         5368 S E64+NT
               E ISOFLAVONE/CT
```

```
                E E5+ALL
L27         687 S E1,E2,E3,E4
L28       26962 S FLAVANOID OR FLAVONOID OR ISOFLAVONE OR ISO FLAVONE
                E ANTIOXIDANT/CT
                E E11+ALL
L29       40491 S E5
                SEL DN 4
L30         496 S L7 OR L3 OR L4
L31          74 S L22 AND L30
L32          55 S L23 AND L31
L33          74 S L31,L32
L34           5 S L24-L29 AND L33
L35          39 S L24-L29 AND L23
L36          37 S L35 NOT L34
L37          69 S L33 NOT L34-L36
                SEL DN 1 6 8 9 12 20 39  60
L38           5 S E2-E6 AND L37
                E ELNAGGAR/AU
                E EL NAGGAR/AU
L39          37 S E58,E63-E65
                E NAGGAR/AU
                E MAWAHAB/AU
                E MOUSA A/AU
L40          16 S E3
L41           1 S E11
L42           4 S E17,E19,E20
L43          58 S L39-L42
L44           1 S L43 AND L7-L38
L45           0 S L39 AND L40-L42
                SEL HIT RN L38

     FILE 'REGISTRY' ENTERED AT 13:39:50 ON 02 FEB 2002
L46           5 S E1-E5
L47           6 S L1,L3,L6,L46

     FILE 'REGISTRY' ENTERED AT 13:40:24 ON 02 FEB 2002


=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:40:37 ON 02 FEB 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 1 Feb 2002  VOL 136 ISS 6
FILE LAST UPDATED: 30 Jan 2002  (20020130/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.
```

(emulsions; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Drug delivery systems
(enteric-coated; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Drug delivery systems
(liposomes, and micelles; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Drug delivery systems
(liqs., dispersions; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Anti-inflammatory agents
(nonsteroidal, conjugates with COX-2 inhibitors; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Drug delivery systems
(solids; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT Drug delivery systems
(solns.; NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT 363-24-6, Prostaglandin E2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT 366803-10-3P 366803-11-4P 366803-12-5P 366803-13-6P 366803-14-7P
366803-15-8P 366803-16-9P 366803-17-0P 366803-18-1P 366803-19-2P
378784-55-5P 378784-56-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NSAID-COX-2 inhibitor conjugates, and therapeutic use)
IT **50-78-2D, Aspirin**, conjugates with COX-2 inhibitors 53-86-1D, Indomethacin, conjugates with COX-2 inhibitors 54-21-7D, Sodium salicylate, conjugates with COX-2 inhibitors 61-68-7D, Mefenamic acid, conjugates with COX-2 inhibitors 103-90-2D, Acetaminophen, conjugates with COX-2 inhibitors 552-94-3D, Salsalate, conjugates with COX-2 inhibitors 2016-36-6D, Choline salicylate, conjugates with COX-2 inhibitors, biological studies 3615-24-5D, Ramifenazone, conjugates with COX-2 inhibitors 5104-49-4D, Flurbiprofen, conjugates with COX-2 inhibitors 6385-02-0D, Meclofenamate sodium, conjugates with COX-2 inhibitors 15307-86-5D, Diclofenac, conjugates with COX-2 inhibitors 15687-27-1D, Ibuprofen, conjugates with COX-2 inhibitors 18917-89-0D, Magnesium salicylate, conjugates with COX-2 inhibitors 21256-18-8D, Oxaprozin, conjugates with COX-2 inhibitors 22071-15-4D, Ketoprofen, conjugates with COX-2 inhibitors 22204-53-1D, Naproxen, conjugates with COX-2 inhibitors 22494-42-4D, Diflunisal, conjugates with COX-2 inhibitors 26171-23-3D, Tolmetin, conjugates with COX-2 inhibitors 31842-01-0D, Indoprofen, conjugates with COX-2 inhibitors 33005-95-7D, Tiaprofenic acid, conjugates with COX-2 inhibitors 34597-40-5D, conjugates with COX-2 inhibitors 36322-90-4D, Piroxicam, conjugates with COX-2 inhibitors 38194-50-2D, Sulindac, conjugates with COX-2 inhibitors 41340-25-4D, Etodolac, conjugates with COX-2 inhibitors 42924-53-8D, Nabumetone, conjugates with COX-2 inhibitors 51803-78-2D, Nimesulide, conjugates with COX-2 inhibitors 53716-49-7D, Carprofen, conjugates with COX-2 inhibitors 64425-90-7D, conjugates with COX-2 inhibitors, biological studies

70374-39-9D, Lornoxicam, conjugates with **COX-2** inhibitors 71125-38-7D, Meloxicam, conjugates with **COX-2** inhibitors 74103-07-4D, Ketorolac tromethamine, conjugates with **COX-2** inhibitors 80937-31-1D, Flosulide, conjugates with **COX-2** inhibitors **162011-90-7D**, **Rofecoxib**, and derivs., conjugates with NSAIDS **169590-42-5D**, **Celecoxib**, and derivs., conjugates with NSAIDS 181695-72-7D, Valdecoxib, and derivs., conjugates with NSAIDS
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID-**COX-2** inhibitor conjugates, and therapeutic use)

IT **329900-75-6**, **Cyclooxygenase 2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, conjugates with NSAIDs; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)

IT **50-78-2**, **Aspirin** 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1, Naproxen 181695-81-8 219679-59-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)

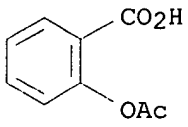
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

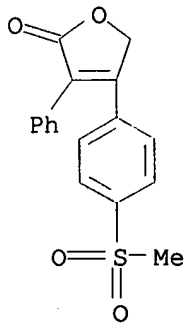
(1) Hellberg; US 5607966 A 1997 HCAPLUS
(2) Horrobin; US 5603959 A 1997 HCAPLUS
(3) Masferrer; US 6025353 A 2000

IT **50-78-2D**, **Aspirin**, conjugates with **COX-2** inhibitors **162011-90-7D**, **Rofecoxib**, and derivs., conjugates with NSAIDS **169590-42-5D**, **Celecoxib**, and derivs., conjugates with NSAIDS
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NSAID-**COX-2** inhibitor conjugates, and therapeutic use)

RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

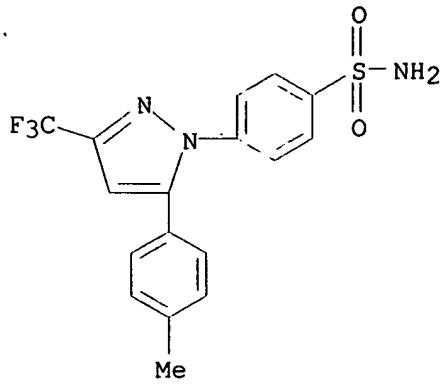
=> d all hitstr tot

L48 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:903700 HCAPLUS
DN **136:15235**
TI Protected forms of a conjugate combination of nonsteroidal antiinflammatory drugs (NSAIDs) and **cyclooxygenase 2** (**COX-2**) inhibitors, and their therapeutic use
IN Lai, Ching-San; Wang, Tingmin
PA Medinox, Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N037-36
ICS A01N037-18; A01N031-16; A01N037-10; A01N037-44; A01N043-38; A61K031-40
CC 1-7 (Pharmacology)
Section cross-reference(s): 28
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001093680	A1	20011213	WO 2001-US17480	20010530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6306842	B1	20011023	US 2000-586344	20000602
PRAI US 2000-586344	A1	20000602		
US 2000-588993	A1	20000606		

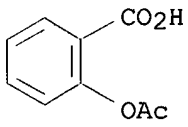
AB The invention provides conjugates of a combination of pharmacol. active agents (e.g., NSAIDs and selective **COX-2** inhibitors). The conjugates provide a new class of pharmacol. active agents (e.g., anti-inflammatory agents) which provide the therapeutic benefits of both NSAIDs and selective **COX-2** inhibitors, while causing a much lower incidence of side-effects then are typically obsd. with such agents due to the protective effects imparted by modifying the pharmacol. active agents.
ST NSAID **COX2** inhibitor conjugate prepn therapeutic; nonsteroidal antiinflammatory drug **cyclooxygenase 2** inhibitor conjugate therapeutic
IT Anti-infective agents
Anti-inflammatory agents
Antiarthritics
Drug delivery systems
(NSAID-**COX-2** inhibitor conjugates, and therapeutic use)
IT Arthritis
(adjuvant; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)
IT Toxicity
(drug; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)
IT Drug delivery systems

yl]- (9CI) (CA INDEX NAME)



IT **329900-75-6, Cyclooxygenase 2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, conjugates with NSAIDs; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)
RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **50-78-2, Aspirin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; NSAID-**COX-2** inhibitor conjugates, and therapeutic use)
RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



L48 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:772128 HCAPLUS
DN **135:298780**
TI Conjugates of antiinflammatory or other pharmacologically active agents, their preparation, and their therapeutic use
IN Lai, Ching-San; Wang, Tingmin
PA Medinox, Inc., USA
SO U.S., 10 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A01N037-36
ICS A01N043-00; A01N051-00; A01N037-10; A01N037-18
NCL 514159000
CC 1-7 (Pharmacology)
Section cross-reference(s): 28
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6306842	B1	20011023	US 2000-586344	20000602
WO 2001093680	A1	20011213	WO 2001-US17480	20010530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-586344 A1 20000602
US 2000-588993 A1 20000606

AB Conjugates of a combination of pharmacol. active agents (e.g., NSAIDs and selective **COX-2** inhibitors) are provided. These conjugates provide a new class of pharmacol. active agents (e.g., anti-inflammatory agents) which provide the therapeutic benefits of both NSAIDs and selective **COX-2** inhibitors, while causing a much lower incidence of side-effects then are typically obsd. with such agents due to the protective effects imparted by modifying the pharmacol. active agents.

ST NSAID **COX2** inhibitor conjugate prepn antiinflammatory; drug conjugate adverse effect redn

IT Anti-infective agents
Anti-inflammatory agents
Drug delivery systems
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Toxicity
(drug; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(emulsions; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(enteric-coated; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(liposomes, and micelles; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(liqs., dispersions; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Anti-inflammatory agents
(nonsteroidal, **COX-2** inhibitor conjugates; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(solids; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT Drug delivery systems
(solns.; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT 181695-81-8P 219679-59-1P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT 366803-10-3P 366803-11-4P 366803-12-5P 366803-13-6P 366803-14-7P
366803-15-8P 366803-16-9P 366803-17-0P 366803-18-1P 366803-19-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT **50-78-2D, Aspirin, COX-2** inhibitor
conjugates 53-86-1D, Indomethacin, **COX-2** inhibitor
conjugates 54-21-7D, Sodium salicylate, **COX-2**
inhibitor conjugates 61-68-7D, Mefenamic acid, **COX-2**
inhibitor conjugates 103-90-2D, Acetaminophen, **COX-2**

inhibitor conjugates 552-94-3D, Salsalate, **COX-2** inhibitor conjugates 2016-36-6D, Choline salicylate, **COX-2** inhibitor conjugates, biological studies 5104-49-4D, Flurbiprofen, **COX-2** inhibitor conjugates 6385-02-0D, Meclofenamate sodium, **COX-2** inhibitor conjugates 15307-86-5D, Diclofenac, **COX-2** inhibitor conjugates 15687-27-1D, Ibuprofen, **COX-2** inhibitor conjugates 18917-89-0D, Magnesium salicylate, **COX-2** inhibitor conjugates 21256-18-8D, Oxaprozin, **COX-2** inhibitor conjugates 22071-15-4D, Ketoprofen, **COX-2** inhibitor conjugates 22204-53-1D, Naproxen, **COX-2** inhibitor conjugates 22494-42-4D, Diflunisal, **COX-2** inhibitor conjugates 26171-23-3D, Tolmetin, **COX-2** inhibitor conjugates 31842-01-0D, Indoprofen, **COX-2** inhibitor conjugates 33005-95-7D, Tiaprofenic acid, **COX-2** inhibitor conjugates 34597-40-5D, **COX-2** inhibitor conjugates 36322-90-4D, Piroxicam, **COX-2** inhibitor conjugates 38194-50-2D, Sulindac, **COX-2** inhibitor conjugates 41340-25-4D, Etodolac, **COX-2** inhibitor conjugates 42924-53-8D, Nabumetone, **COX-2** inhibitor conjugates 51803-78-2D, Nimesulide, **COX-2** inhibitor conjugates 53716-49-7D, Carprofen, **COX-2** inhibitor conjugates 64425-90-7D, **COX-2** inhibitor conjugates, biological studies 70374-39-9D, Lornoxicam, **COX-2** inhibitor conjugates 71125-38-7D, Meloxicam, **COX-2** inhibitor conjugates 74103-07-4D, Ketorolac tromethamine, **COX-2** inhibitor conjugates 80937-31-1D, Flosulide, **COX-2** inhibitor conjugates **162011-90-7D, Rofecoxib**, NSAID conjugates **169590-42-5D, Celecoxib**, NSAID conjugates 181695-72-7D, Valdecoxib, NSAID conjugates
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT 363-24-6, Prostaglandin E2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

IT **329900-75-6, Cyclooxygenase 2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, NSAID conjugates; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

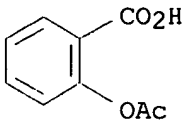
IT **50-78-2, Aspirin** 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1, Naproxen
RL: RCT (Reactant)
(reaction; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

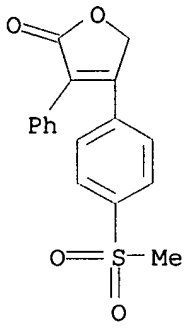
RE

(1) Bjarnason; Gastroenterology 1993, V104, P1832 MEDLINE
(2) Carson; Arch Intern Med 1987, V147, P1054 MEDLINE
(3) Glaser; European Journal of Pharmacology 1995, V281, P107 HCAPLUS
(4) Graham; Clin Pharmacol Ther 1985, V38, P65 MEDLINE
(5) Hellberg; US 5607966 1997 HCAPLUS
(6) Horrobin; US 5603959 1997 HCAPLUS
(7) John, L; Gastroenterology 1997, V112, P1000
(8) Kaplan-Machlis And Klostermeyer; The Annals of Pharmacotherapy 1999, V33, P979
(9) Kargman; Gastroenterology 1996, V111, P445 HCAPLUS
(10) Masferrer; US 6025353 2000
(11) Meade; The Journal of Biological Chemistry 1993, V268/9, P6610
(12) Mitchell; Proc Natl Acad Sci USA 1994, V90, P11693
(13) Onoe; The Journal of Immunology 1996, V156, P758 HCAPLUS
(14) Slater; Am J Obstet Gynecol 1995, V172, P77 HCAPLUS
(15) Soll; Annals of Internal Medicine 1991, V114, P307 MEDLINE

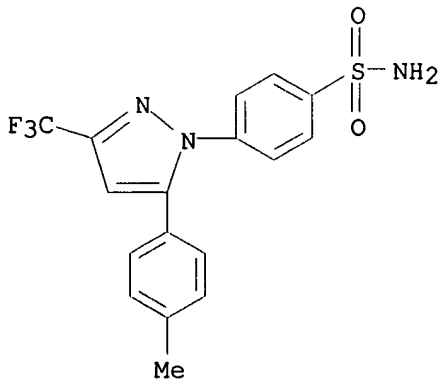
IT **50-78-2D, Aspirin, COX-2** inhibitor conjugates **162011-90-7D, Rofecoxib,** NSAID conjugates **169590-42-5D, Celecoxib,** NSAID conjugates
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)
RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



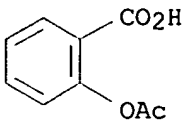
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



IT **329900-75-6, Cyclooxygenase 2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, NSAID conjugates; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)
RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **50-78-2, Aspirin**

RL: RCT (Reactant)
(reaction; conjugates of antiinflammatory or other pharmacol. active agents, prepn., and therapeutic use)
RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



L48 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:606181 HCAPLUS
DN **135:338932**
TI Lack of cross-reactivity between **rofecoxib** and **aspirin** in **aspirin**-sensitive patients with asthma
AU Stevenson, Donald D.; Simon, Ronald A.
CS Division of Allergy, Asthma and Immunology, Department of Medicine, Scripps Clinic and The Scripps Research Institute, La Jolla, CA, 92037, USA
SO J. Allergy Clin. Immunol. (2001), 108(1), 47-51
CODEN: JACIBY; ISSN: 0091-6749
PB Mosby, Inc.
DT Journal
LA English
CC 1-7 (Pharmacology)
AB Patients with **aspirin**-sensitive respiratory disease experience cross-reactions to all nonsteroidal anti-inflammatory drugs, which inhibit **cyclooxygenase** enzymes. With the introduction of antiarthritis drugs, which selectively inhibit **cyclooxygenase-2**, questions are raised as to whether cross-reactivity occurs between **aspirin** and these new **cyclooxygenase-2** inhibitors. The goal of this study was to det. whether **rofecoxib** cross-reacts in **aspirin**-sensitive patients with asthma. Sixty patients with asthma underwent double-blinded, placebo-controlled oral challenges with **rofecoxib** (12.5 mg, 25 mg, and **2** placebos) over 48 h in our General Clin. Research Center. The next day, **aspirin** sensitivity was proven in each of the 60 patients through use of single-blinded oral **aspirin** challenges. None of the 60 patients experienced any symptoms, changes in nasal examn. findings, or declines in FEV1 values during their challenges with **rofecoxib**. All 60 patients experienced typical naso-ocular and asthmatic reactions to **aspirin** with a mean provoking dose of 61 mg. The exact **1** -sided CI for the probability of **rofecoxib** inducing cross-reactions in **aspirin**-sensitive patients with asthma is calcd. to be between 0% and 0.05%. Given that none of the 60 patients reacted to **rofecoxib** and given the statistical power of this large sample size, we conclude that cross-reactivity between **aspirin** and **rofecoxib** does not occur in patients with **aspirin**-sensitive respiratory disease. This does not exclude **rofecoxib** from participating in other types of reactions, including immune recognition after prior treatment with the drug. From the standpoint of the mechanisms involved in **aspirin**-induced respiratory reactions, this study strongly supports inhibition of **cyclooxygenase-1** as the essential initiator of these types of reactions.
ST **rofecoxib aspirin** crossreactivity asthma
IT Anti-inflammatory agents
Antiarthritics
Asthma
(**rofecoxib** cross-reactivity in **aspirin**-sensitive humans with asthma)
IT **329900-75-6, Cyclooxygenase-2**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **rofecoxib** cross-reactivity in **aspirin**
-sensitive humans with asthma)

IT **50-78-2, Aspirin 162011-90-7,**
Rofecoxib
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rofecoxib** cross-reactivity in **aspirin**-sensitive
humans with asthma)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Andri, L; Ann Allergy 1994, V72, P29 MEDLINE
(2) Dahlen, B; N Engl J Med 2001, V344, P142 MEDLINE
(3) Demoly, P; Am J Respir Crit Care Med 1997, V155, P670 MEDLINE
(4) Ferreri, N; Am Rev Respir Dis 1988, V137, P847 MEDLINE
(5) Fischer, A; J Allergy Clin Immunol 1994, V94, P1046 MEDLINE
(6) Hawkey, C; Lancet 1999, V353, P307 HCAPLUS
(7) Kosnik, M; Allergy 1998, V53, P1231 MEDLINE
(8) Kuehl, F; Biochem Pharmacol 1984, V33, P1 HCAPLUS
(9) Lehmann, E; Testing statistical hypotheses. 2nd ed 1986
(10) Medical Economics Company; Physicians Drug Reference. 55th ed 2001, P2050
(11) Nasser, S; Eicosanoids, aspirin and asthma 1998, P317 HCAPLUS
(12) Nizankowska, E; Ann Allergy 1989, V63, P159 MEDLINE
(13) Pauls, J; Ann Allergy Asthma Immunol 2000, V85, P40 HCAPLUS
(14) Settipane, R; J Allergy Clin Immunol 1989, V84, P26 MEDLINE
(15) Stevenson, D; Allergy: principles and practice. 5th ed 1998, P1225
(16) Stevenson, D; Ann Allergy Asthma Immunol 2000, V85, P477 HCAPLUS
(17) Stevenson, D; J Allergy Clin Immunol 1990, V86, P749 MEDLINE
(18) Stevenson, D; J Allergy Clin Immunol 2000, V105, PS273
(19) Szczeklik, A; Am J Respir Crit Care Med 1996, V153, P567 MEDLINE
(20) Szczeklik, A; Clin Exp Allergy 2001, V31, P219 HCAPLUS
(21) Szczeklik, A; Eur Respir J 1990, V3, P588 HCAPLUS
(22) Szczeklik, A; J Allergy Clin Immunol 1977, V60, P276 MEDLINE
(23) Szczeklik, A; J Allergy Clin Immunol 1999, V104, P5 MEDLINE
(24) Szczeklik, A; Thorax 1979, V34, P654 MEDLINE
(25) Yoshida, S; J Allergy Clin Immunol 2000, V106, P1203

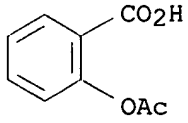
IT **329900-75-6, Cyclooxygenase-2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **rofecoxib** cross-reactivity in **aspirin**
-sensitive humans with asthma)

RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

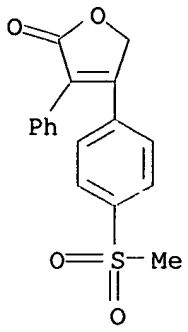
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **50-78-2, Aspirin 162011-90-7,**
Rofecoxib
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**rofecoxib** cross-reactivity in **aspirin**-sensitive
humans with asthma)

RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



L48 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:880190 HCAPLUS
DN **135:40445**
TI A new **cyclooxygenase-2** inhibitor, **rofecoxib** (**VIOXX**), did not alter the antiplatelet effects of low-dose **aspirin** in healthy volunteers
AU Greenberg, Howard E.; Gottesdiener, Keith; Huntington, Martha; Wong, Peggy; Larson, Pat; Wildonger, Lynn; Gillen, Lisa; Dorval, Ellen; Waldman, Scott A.
CS Division of Clinical Pharmacology, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SO Journal of Clinical Pharmacology (2000), 40(12, Pt. 2), 1509-1515
CODEN: JCPCBR; ISSN: 0091-2700
PB Sage Publications
DT Journal
LA English
CC 1-4 (Pharmacology)
AB This study examd. whether **rofecoxib** (**VIOXX**), a new specific inhibitor of **cyclooxygenase-2** (**COX-2**), would interfere with the desired antiplatelet effects of **aspirin**. The effects of **rofecoxib** on inhibition of ex vivo serum-generated TXB2 and platelet aggregation by low doses (81 mg) of **aspirin** were examd. in healthy volunteers. Subjects received 50 mg **rofecoxib** or placebo for 10 days in a blinded fashion. The subjects also received 81 mg **aspirin** once on each of days 4-10 in an open-label fashion. **Rofecoxib** alone did not inhibit serum TXB2 prodn. or platelet aggregation. In addn., **rofecoxib** did not alter the antiplatelet effects of low-dose **aspirin** (inhibition of platelet aggregation and TXB2 prodn.). **Rofecoxib** was generally well tolerated when administered alone or in combination with low-dose **aspirin**.
ST **cyclooxygenase** inhibitor **rofecoxib** interaction **aspirin** platelet aggregation
IT Platelet (blood)
(aggregation; **cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)
IT Drug interactions
Platelet (blood)
(**cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)
IT **162011-90-7, Rofecoxib**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)
IT **50-78-2, Aspirin**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); BIOL (Biological study); PROC (Process)
(**cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)

IT **329900-75-6, cyclooxygenase 2**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

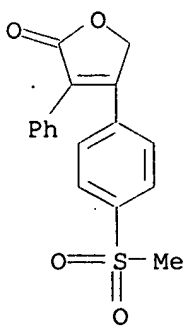
RE

(1) Akarasereenont, P; Br J Pharmacol 1994, V113, P1522 HCAPLUS
(2) Berenbaum, F; Exp Cell Res 1996, V222, P379 HCAPLUS
(3) Blanco, A; Biochem J 1995, V312, P419 HCAPLUS
(4) Chan, C; J Pharmacol Exp Ther 1995, V274(3), P1531 HCAPLUS
(5) Copeland, R; Proc Natl Acad Sci USA 1994, V91, P11202 HCAPLUS
(6) Crofford, L; J Clin Invest 1994, V93, P1095 HCAPLUS
(7) De Caterina, R; Thromb Haemost 1985, V54(2), P528 MEDLINE
(8) Department of Drug Metabolism, Merck Research Laboratories; MRL Preclinical Report: An in vitro plasma protein binding displacement interaction study with [14C]rofecoxib and [14C]salicylic acid
(9) Depre, M; Eur J Pharmacol 2000, V56, P167 HCAPLUS
(10) Dubois, R; Gastroenterology 1996, V110(4), P1259 HCAPLUS
(11) Eberhart, C; Gastroenterology 1994, V107(4), P1183 MEDLINE
(12) Ehrich, E; Clin Pharm Ther 1999, V65, P336 HCAPLUS
(13) Hla, T; Proc Natl Acad Sci USA 1992, V89, P7384 HCAPLUS
(14) Holtzman, M; J Biol Chem 1992, V267(30), P21438 HCAPLUS
(15) Lee, S; J Biol Chem 1992, V267(36), P25934 HCAPLUS
(16) Li, C; J Med Chem 1995, V38(25), P4897 HCAPLUS
(17) Lyons-Giordano, B; Exp Cell Res 1993, V206, P58 HCAPLUS
(18) Masferrer, J; Proc Natl Acad Sci USA 1994, V91, P3228 HCAPLUS
(19) Meade, E; J Biol Chem 1993, V268(9), P6610 HCAPLUS
(20) Merck and Co, Inc; VIOXX Package Insert
(21) Mitchel, J; Proc Natl Acad Sci USA 1994, V90, P11693
(22) Patrignani, P; J Clin Invest 1982, V69, P1366 HCAPLUS
(23) Pritchard, K; J Biol Chem 1994, V269(11), P8504 HCAPLUS
(24) Sano, H; Cancer Res 1995, V55, P3785 HCAPLUS
(25) Sirois, J; J Biol Chem 1992, V267(16), P11586 HCAPLUS
(26) Spaziani, E; Prostaglandins 1996, V51, P215 HCAPLUS
(27) Vadas, P; Eur J Biochem 1996, V235, P557 HCAPLUS

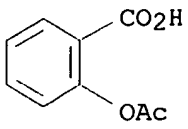
IT **162011-90-7, Rofecoxib**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)

RN 162011-90-7 HCAPLUS

CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



IT **50-78-2, Aspirin**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)
RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



IT **329900-75-6, cyclooxygenase 2**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **cyclooxygenase-2** inhibitor **rofecoxib** (**VIOXX**) did not alter the antiplatelet effects of low-dose **aspirin** in humans)
RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L48 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:594916 HCAPLUS
DN **131:209130**
TI Combination therapy and composition using an antiplatelet agent and a **COX-2** inhibitor for acute coronary ischemic syndrome and related conditions
IN Nichtberger, Steven A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-10
ICS A61K031-16; A61K031-34; A61K031-40; A61K031-42; A61K031-44; A61K031-55; A61K031-225; A61K031-425; A61K031-445; A61K031-505; A61K038-16; A01N037-02; A01N037-06; A01N037-18; A01N041-10; A01N043-08; A01N043-36; A01N043-40; A01N043-42
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9945913	A1	19990916	WO 1999-US5063	19990309
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1061908	A1	20001227	EP 1999-911208	19990309
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	US 6136804	A	20001024	US 1999-267287	19990312
PRAI	US 1998-77900	P	19980313		
	GB 1998-15857	A	19980721		
	WO 1999-US5063	W	19990309		

AB A method for treating, preventing, or reducing the risk of developing a condition selected from acute coronary ischemic syndrome, thrombosis, thromboembolism, thrombotic occlusion and reocclusion, restenosis, transient ischemic attack, and first or subsequent thrombotic stroke, in a

patient comprises administering to the patient a therapeutically effective amt. of an antiplatelet agent in combination with a therapeutically effective amt. of a **COX-2** inhibitor. The invention also provides a pharmaceutical compn. comprising a therapeutically effective amt. of a **COX-2** inhibitor, or a pharmaceutically acceptable salt thereof, and an antiplatelet agent, or a pharmaceutically acceptable salt thereof.

ST antiplatelet agent combination acute coronary ischemic syndrome; **COX2** inhibitor combination acute coronary ischemic syndrome; cardiovascular combination **cyclooxygenase 2** inhibitor antiplatelet agent

IT Heart, disease
(angina pectoris; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Anti-ischemic agents
Anticoagulants
Cardiovascular agents
Drug delivery systems
Platelet aggregation inhibitors
(antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(capsules; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Heart, disease
(infarction, first and subsequent Q-wave; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(injections, i.v.; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Blood vessel, disease
(occlusion, and reocclusion; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(oral; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(prodrugs; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Artery, disease
(restenosis; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(solns., oral; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

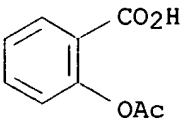
IT Brain, disease
(stroke, thrombotic; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

IT Drug delivery systems
(suspensions, oral; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)

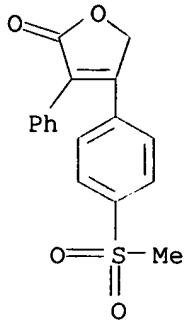
IT Drug delivery systems
(tablets; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome

and related conditions)
IT Embolism
(thromboembolism; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.IIb.beta.3, antagonists; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
IT **39391-18-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**2**, inhibitors; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
IT **50-78-2**, **Aspirin** 58-32-2, Dipyridamole 55142-85-3, Ticlopidine 105806-65-3 105806-65-3D, esters 113665-84-2, Clopidogrel 142373-60-2 142373-60-2D, esters 144412-49-7 144412-49-7D, esters 146144-48-1 146144-48-1D, esters 162011-83-8 **162011-90-7** 163212-43-9 163212-43-9D, esters 169237-80-3 169237-80-3D, esters 176022-59-6 178402-36-3 185147-73-3 189954-66-3 189954-87-8 189954-93-6 189954-96-9 189956-36-3 190966-03-1 190966-25-7 190966-32-6 202409-31-2 202409-33-4 205385-39-3 205385-39-3D, esters 205385-41-7 205385-41-7D, esters 208260-66-6 208260-66-6D, esters 212126-32-4 223240-38-8 223240-38-8D, esters 223240-39-9 223240-39-9D, esters 223663-01-2 223663-03-4 243637-40-3D, esters
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Blackburn; US 5250679 A 1993 HCAPLUS
(2) Bovy; US 5344957 A 1994 HCAPLUS
(3) G D Searle & Co; WO 9735592 A1 1997 HCAPLUS
(4) Gyogyszerkutato Intezet Kft; WO 9746576 A1 1997 HCAPLUS
(5) Merck Frosst Canada Inc; WO 9714691 A1 1997 HCAPLUS
(6) Merck Frosst Canada Inc; WO 9803484 A1 1998 HCAPLUS
(7) Nicox S A; WO 9716405 A1 1997 HCAPLUS
(8) Szalony, J; Circulation 1995, V91(2), P411 HCAPLUS
IT **39391-18-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**2**, inhibitors; antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
RN 39391-18-9 HCAPLUS
CN Synthetase, prostaglandin endoperoxide (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **50-78-2**, **Aspirin 162011-90-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiplatelet agent-**cyclooxygenase-2** inhibitor combination for treatment of acute coronary ischemic syndrome and related conditions)
RN 50-78-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)



RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



=> fil medline
FILE 'MEDLINE' ENTERED AT 13:54:39 ON 02 FEB 2002

FILE LAST UPDATED: 1 FEB 2002 (20020201/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all

L70 ANSWER 1 OF 1 MEDLINE
AN 2002056162 MEDLINE
DN **21624531** PubMed ID: **11752357**
TI Cyclooxygenase inhibitors and the antiplatelet effects of **aspirin**
.
CM Comment in: N Engl J Med. 2001 Dec 20;345(25):1844-6
AU Catella-Lawson F; Reilly M P; Kapoor S C; Cucchiara A J; DeMarco S; Tournier B; Vyas S N; FitzGerald G A
CS EUPenn Group of Investigators, Center for Experimental Therapeutics, University of Pennsylvania School of Medicine, Philadelphia 19104-6084, USA.
NC HL 5400 (NHLBI)
HL 62250 (NHLBI)
M01RR00040 (NCRR)
SO NEW ENGLAND JOURNAL OF MEDICINE, (2001 Dec 20) 345 (25) 1809-17.
Journal code: 0255562. ISSN: 0028-4793.
CY United States
DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200201
ED Entered STN: 20020125
Last Updated on STN: 20020128
Entered Medline: 20020123
AB BACKGROUND: Patients with arthritis and vascular disease may receive both low-dose **aspirin** and other nonsteroidal antiinflammatory drugs. We therefore investigated potential interactions between **aspirin** and commonly prescribed arthritis therapies METHODS: We administered the following combinations of drugs for six days: **aspirin** (81 mg every morning) two hours before ibuprofen (400 mg every morning) and the same medications in the reverse order; **aspirin** two hours before acetaminophen (1000 mg every morning) and the same medications in the reverse order; **aspirin** two hours before the cyclooxygenase-2 inhibitor **rofecoxib** (25 mg every morning) and the same medications in the reverse order; enteric-coated **aspirin** two hours before ibuprofen (400 mg three times a day); and enteric-coated **aspirin** two hours before delayed-release diclofenac (75 mg twice daily) RESULTS: Serum thromboxane B(2) levels (an index of cyclooxygenase-1 activity in platelets) and platelet aggregation were maximally inhibited 24 hours after the administration of **aspirin** on day 6 in the subjects who took **aspirin** before a single daily dose of any other drug, as well as in those who took **rofecoxib** or acetaminophen before taking **aspirin**. In contrast, inhibition of serum thromboxane B(2) formation and platelet aggregation by **aspirin** was blocked when a single daily dose of ibuprofen was given before **aspirin**, as well as when multiple daily doses of ibuprofen were given. The concomitant administration of **rofecoxib** , acetaminophen, or diclofenac did not affect the pharmacodynamics of **aspirin** CONCLUSIONS: The concomitant administration of ibuprofen but not **rofecoxib**, acetaminophen, or diclofenac antagonizes the irreversible platelet inhibition induced by **aspirin**. Treatment with ibuprofen in patients with increased cardiovascular risk may limit the cardioprotective effects of **aspirin**.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Acetaminophen: PD, pharmacology
Adult
Analgesics, Non-Narcotic: PD, pharmacology
*Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology
Aspirin: AI, antagonists & inhibitors
***Aspirin: PD, pharmacology**
Cross-Over Studies
***Cyclooxygenase Inhibitors: PD, pharmacology**
Diclofenac: PD, pharmacology
Dinoprostone: BL, blood
Drug Interactions
Drug Therapy, Combination
Ibuprofen: PD, pharmacology
*Isoenzymes: AI, antagonists & inhibitors
Lactones: PD, pharmacology
Middle Age
*Platelet Aggregation: DE, drug effects
*Platelet Aggregation Inhibitors: PD, pharmacology
Prostaglandin-Endoperoxide Synthase
Thromboxane B2: BL, blood
RN 103-90-2 (Acetaminophen); 15307-86-5 (Diclofenac); 15687-27-1 (Ibuprofen); 363-24-6 (Dinoprostone); **50-78-2 (Aspirin)**; 54397-85-2 (Thromboxane B2)
CN 0 (Analgesics, Non-Narcotic); 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Cyclooxygenase Inhibitors); 0 (Isoenzymes); 0 (Lactones); 0 (Platelet Aggregation Inhibitors); 0 (**rofecoxib**); EC 1.14.99.- (cyclooxygenase 1); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

=> fil biosis
FILE 'BIOSIS' ENTERED AT 14:09:14 ON 02 FEB 2002

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 30 January 2002 (20020130/ED)

The BIOSIS file has been reloaded. Enter HELP RLOAD and HELP REINDEXING
for details.

=> d all tot

L95 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:110192 BIOSIS
DN PREV200100110192
TI Anti-inflammatory **dosages** of **aspirin**, or
celecoxib, versus antithrombotic dose of **aspirin** for
reducing acute silent ischemia.
AU Gurfinkel, Enrique P. (1); Bozovich, Gerardo E. (1); Litvak Bruno, Marcos
R.; Schnidt, Jose L.; Scazziota, Alejandra
CS (1) Favaloro Fdn, Buenos Aires Argentina
SO Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.500.
print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans,
Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DT Conference
LA English
SL English
CC Pharmacology - General *22002
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Cardiovascular System - Heart Pathology *14506
Cardiovascular System - Blood Vessel Pathology *14508
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Cardiovascular System *22010
IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences);
Pharmacology
IT Diseases
silent myocardial ischemia: drug treatment, heart disease, vascular
disease
IT Chemicals & Biochemicals
Celecoxib: cardiovascular - drug, cyclooxygenase-2 inhibitor;
aspirin: antiinflammatory dosage, antithrombotic dosage,
cardiovascular - drug, comparative dosage study
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **169590-42-5 (CELECOXIB)**
50-78-2 (ASPIRIN)

L95 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:538424 BIOSIS

DN PREV199900538424
TI Thrombosis and ischemia in patients with systemic **lupus** erythematosus treated with **celecoxib**: A series of two cases.
AU Gupta, Samardeep (1); McCune, W. J. (1); Kaplan, Mariana J. (1); McDonagh, Kevin T. (1); Schmaier, Alvin H. (1); Crofford, Leslie J. (1)
CS (1) Ann Arbor, MI USA
SO Arthritis & Rheumatism, (Sept., 1999) Vol. 42, No. 9 SUPPL., pp. S149. Meeting Info.: 63rd Annual Scientific Meeting of the American College of Rheumatology and the 34th Annual Scientific Meeting of the Association of Rheumatology Health Professionals Boston, Massachusetts, USA November 13-17, 1999
ISSN: 0004-3591.
DT Conference
LA English
CC Pharmacology - General *22002
Biochemical Studies - General *10060
Cardiovascular System - General; Methods *14501
Toxicology - General; Methods and Experimental *22501
Immunology and Immunochemistry - General; Methods *34502
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Pharmacology; Rheumatology (Human Medicine, Medical Sciences)
IT Diseases
ischemia: vascular disease; systemic lupus erythematosus: connective tissue disease, immune system disease; thrombosis: vascular disease
IT Chemicals & Biochemicals
celecoxib: COX-2 inhibitor, antiarthritic - drug, immunosuppressant - drug, enzyme inhibitor - drug; low-dose **aspirin**: anticoagulant - drug; prostaglandins; thromboxanes
IT Alternate Indexing
Ischemia (MeSH); Lupus Erythematosus, Systemic (MeSH); Thrombosis (MeSH)
IT Methods & Equipment
drug treatment: therapeutic method
IT Miscellaneous Descriptors
drug adverse events; risk factors; Meeting Abstract; Meeting Poster
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN **169590-42-5** (**CELECOXIB**)
66719-58-2 (THROMBOXANES)

L95 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:290842 BIOSIS
DN PREV199900290842
TI Influence of H. **pylori** (Hp) infection and/or low dose **aspirin** (AASA) on gastroduodenal ulceration in patients treated wigh placebo, **celecoxib** or NSAIDs.
AU Goldstein, Jay L. (1); Agrawal, N. M. (1); Silverstein, F. (1); Verburg, K. M. (1); Burr, A. M. (1); Hubbard, R. C. (1); Zhao, W. (1); Geis, G. S. (1)
CS (1) Univ of Illihois at Chicago, Chicago, IL USA
SO Gastroenterology, (April, 1999) Vol. 116, No. 4 PART 2, pp. A174. Meeting Info.: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference

LA English
CC Pharmacology - General *22002
Biochemical Studies - General *10060
Digestive System - General; Methods *14001
Medical and Clinical Microbiology - General; Methods and Techniques *36001
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Aerobic Helical or Vibrioid Gram-Negatives 06210
Hominidae 86215
IT Major Concepts
Infection; Pharmacology
IT Diseases
gastroduodenal ulcer: digestive system disease; Helicobacter pylori infection: bacterial disease, influence
IT Chemicals & Biochemicals
aspirin: influence, low-dose; **celecoxib**: cyclooxygenase-2 inhibitor; non steroidal anti-inflammatory drugs
IT Alternate Indexing
Helicobacter Infections (MeSH)
IT Miscellaneous Descriptors
placebo; Meeting Abstract
ORGN Super Taxa
Aerobic Helical or Vibrioid Gram-Negatives: Eubacteria, Bacteria, Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient; Helicobacter pylori (Aerobic Helical or Vibrioid Gram-Negatives): pathogen
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates
RN **50-78-2 (ASPIRIN)**
169590-42-5 (CELECOXIB)

=> fil wpix
FILE 'WPIX' ENTERED AT 14:24:20 ON 02 FEB 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE LAST UPDATED: 30 JAN 2002 <20020130/UP>
MOST RECENT DERWENT UPDATE 200207 <200207/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SDI'S MAY BE RUN ON EVERY UPDATE OR MONTHLY AS OF JUNE 2001.
(EVERY UPDATE IS THE DEFAULT). FOR PRICING INFORMATION
SEE HELP COST <<<

>>> FOR UP-TO-DATE INFORMATION ABOUT THE DERWENT CHEMISTRY RESOURCE, PLEASE VISIT
http://www.derwent.com/chemistryresource/index.html <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

=> d all abeq tech

L112 ANSWER 1 OF 1 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-536500 [59] WPIX
DNC C2001-159726
TI Method for treating inflammatory disease using a phosphodiesterase (PDE) 4 inhibitor and non-steroidal antiinflammatory drug.
DC B05
IN KANAGY, J M; KEATING, E T
PA (SMIK) SMITHKLINE BEECHAM CORP

CYC 80 .
PI WO 2001058441 A1 20010816 (200159)* EN 10p A61K031-19 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AL AU BA BB BG BR BZ CA CN CZ DZ EE GE GH GM HR HU ID IL IN IS
JP KP KR LC LK LR LT LV MA MG MK MN MX MZ NO NZ PL RO SG SI SK SL
TR TT TZ UA US UZ VN YU ZA
AU 2001072057 A 20010820 (200175) A61K031-19 <--
ADT WO 2001058441 A1 WO 2001-US3972 20010208; AU 2001072057 A AU 2001-72057
20010208
FDT AU 2001072057 A Based on WO 200158441
PRAI US 2000-180879P 20000208
IC ICM A61K031-19
ICS A61K031-40; A61K031-60
AB WO 200158441 A UPAB: 20011012
NOVELTY - Method for treating inflammatory disease by administering a phosphodiesterase (PDE) 4 inhibitor and a non-steroidal antiinflammatory drug (NSAID) in a combined form, separately or sequentially, where the sequential administration is close in time or remote in time.
ACTIVITY - Antiinflammatory; Analgesic; Antirheumatic; Antiarthritic; Osteopathic; Vasotropic.
MECHANISM OF ACTION - PDE 4 inhibitor; **Cyclooxygenase**-1 (**COX**-1) inhibitor; **Cyclooxygenase**-2 (**COX**-2) inhibitor.
PDE activity was assayed using a (3H)cAMP SPA or (3H)cGMP scintillation proximity analysis enzyme assay. A (3H)R-rolipram binding assay was also performed. No activity data was given.
USE - For the treatment of inflammatory diseases e.g. rheumatic disorders such as rheumatoid arthritis, osteoarthritis and spondyloarthropathies and also peri-articular, and soft-tissue rheumatism. The method may also be useful for treating pulmonary diseases.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B05-A01B; B05-A02; B06-H; B07-D02; B07-D08; B10-A10; B10-A15; B10-A22; B10-B04; B10-C03; B10-C04B; B10-E02; B10-F02; B14-C03; B14-C09; B14-D05C; B14-D07A; B14-K01
TECH UPTX: 20011012
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Active Agents: The PDE 4 inhibitor is cis-4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexan-1-carboxylic acid. The antiinflammatory drug is **aspirin**, carprofen, choline salicylate, ketoprofen, magnesium salicylate, salicylamide, salsalate, sodium salicylate, sodium thiosalicylate, meclofenamate sodium, oxyphenbutazone, phenylbutazone, indomethacin, piroxicam, sulindac, tolmetin, tolmetin sodium, mefenamic acid, zomerpirac, ibuprofen, fenoprofen, naproxen, naproxen sodium, diclofenac, flurbiprofen, ketoprofen, ketorolac, trometomol, **celecoxib**, diflunisal and nabumatone.

=> d his

(FILE 'HOME' ENTERED AT 12:35:38 ON 02 FEB 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 12:37:00 ON 02 FEB 2002
L1 1 S ASPIRIN/CN
L2 482.S 50-78-2/CRN
L3 2 S (CELECOXIB OR ROFECOXIB)/CN
L4 10 S (169590-42-5 OR 162011-90-7)/CRN
L5 0 S L2 AND L4
E CYCLOOXYGENASE/CN
L6 3 S E3,E6,E7

FILE 'HCAPLUS' ENTERED AT 12:39:32 ON 02 FEB 2002

```
L7          448 S CELEBREX OR CELECOXIB OR CELOCOXIB OR YM177 OR YM 177 OR SC58
L8         9063 S L6
               E COX
L9          429 S E5
L10        1257 S E52
L11        3342 S COX()(2 OR 1)
L12       15098 S CYCLOOXYGENASE
L13        7592 S CYCLOOXYGENASE(L)2
L14        7109 S CYCLOOXYGENASE(L)1
L15        1073 S PROSTAGLANDIN(L)ENDOPEROXID?(L)(SYNTHETASE OR SYNTHASE)
L16       17880 S L8-L15
L17       14014 S L1
L18        1062 S L2
L19       15320 S ASPIRIN
L20        8244 S (ACETYLSALICYLIC OR ACETYL SALICYLIC)()ACID OR ACETOL
L21        1434 S (ACETOXYBENZOIC OR ACETOXY BENZOIC)()ACID
L22       25229 S L17-L21
L23        2134 S L16 AND L22
               E FLAVANOID/CT
               E E7+ALL
L24           4 S E1
               E E2+ALL
L25       32506 S E4+NT
L26        5368 S E64+NT
               E ISOFLAVONE/CT
               E E5+ALL
L27         687 S E1,E2,E3,E4
L28       26962 S FLAVANOID OR FLAVONOID OR ISOFLAVONE OR ISO FLAVONE
               E ANTIOXIDANT/CT
               E E11+ALL
L29       40491 S E5
               SEL DN 4
L30         496 S L7 OR L3 OR L4
L31          74 S L22 AND L30
L32          55 S L23 AND L31
L33          74 S L31,L32
L34           5 S L24-L29 AND L33
L35          39 S L24-L29 AND L23
L36          37 S L35 NOT L34
L37          69 S L33 NOT L34-L36
               SEL DN 1 6 8 9 12 20 39  60
L38           5 S E2-E6 AND L37
               E ELNAGGAR/AU
               E EL NAGGAR/AU
L39          37 S E58,E63-E65
               E NAGGAR/AU
               E MAWAHAB/AU
               E MOUSA A/AU
L40          16 S E3
L41           1 S E11
L42           4 S E17,E19,E20
L43          58 S L39-L42
L44           1 S L43 AND L7-L38
L45           0 S L39 AND L40-L42
               SEL HIT RN L38

    FILE 'REGISTRY' ENTERED AT 13:39:50 ON 02 FEB 2002
L46           5 S E1-E5
L47           6 S L1,L3,L6,L46

    FILE 'REGISTRY' ENTERED AT 13:40:24 ON 02 FEB 2002

    FILE 'HCAPLUS' ENTERED AT 13:40:37 ON 02 FEB 2002
L48           5 S L38 AND L7-L45

    FILE 'MEDLINE' ENTERED AT 13:42:35 ON 02 FEB 2002
```

```
L49      23676 S L1 OR L2
L50      31217 S L19-L21
L51      31218 S L49,L50
L52        310 S L3 OR L4
L53        560 S L7
L54        560 S L52,L53
L55         71 S L51 AND L54
               E CYCLOOXYGENASE/CT
               E E5+ALL
L56       6496 S L28
               E ANTIOXIDANT/CT
               E E4+ALL
L57      99278 S E7+NT
               E E58+ALL
L58      46425 S E7+NT
               E FLAVANOID/CT
               E FLAVONOID/CT
               E ISOFLAVONE/CT
               E E4+ALL
L59      11629 S E14+NT
L60          3 S L55 AND L56-L59
               E DRUG COMBINATION/CT
               E E6+ALL
L61          0 S E4+NT AND L55
               E DRUG THERAPY, COMBINATION/CT
               E E3+ALL
L62          1 S E4+NT AND L55
L63       4433 S CYCLOOXYGENASE INHIBITORS/CT
L64        685 S L51 AND L63
L65         22 S L64 AND (DRUG THERAPY, COMBINATION+NT OR DRUG COMBINATIONS+NT
L66          0 S L65 AND L57-L59
L67          5 S L65 NOT AB/FA
L68         17 S L65 NOT L67
               SEL DN 1
L69          1 S L68 AND E1-E2
L70          1 S L69,L62

     FILE 'MEDLINE' ENTERED AT 13:54:39 ON 02 FEB 2002

     FILE 'EMBASE' ENTERED AT 13:54:54 ON 02 FEB 2002
L71      58285 S L1 OR L2
L72      60423 S L19-L21
L73      61556 S L71,L72
L74       1279 S L3 OR L4
L75       1364 S L7
L76        423 S L73 AND L74,L75
L77         49 S ((ROFECOXIB OR CELECOXIB)(L)CB)/CT
L78       4344 S ((ACETYLSALICYLIC ACID)(L)CB)/CT
L79         15 S L76 AND L77
L80         24 S L76 AND L78
L81          8 S L79 AND L80
L82       4059 S  (CYCLOOXYGENASE 2 INHIBITOR+NT)/CT
L83        917 S L82 AND L73
L84         50 S L78 AND L83
L85        164 S  ((CYCLOOXYGENASE 2 INHIBITOR+NT)(L)CB)/CT
L86         44 S L85 AND L83
L87         70 S L79,L80,L81,L84,L86
L88         19 S L87 NOT AB/FA
L89         51 S L87 NOT L88

     FILE 'BIOSIS' ENTERED AT 14:04:41 ON 02 FEB 2002
L90      27382 S L73
L91        604 S L3 OR L4 OR L7
L92         68 S L90 AND L91
L93      27458 S L90 OR ASPIRIN?
L94         68 S L93 AND (L3 OR L4 OR L7)
```

```
L95          3 S (DOSAGE OR PYLORI OR LUPUS)/TI AND L94

     FILE 'BIOSIS' ENTERED AT 14:09:14 ON 02 FEB 2002
L96         14 S L93 AND (ELNAGGAR ? OR EL NAGGAR ? OR NAGGAR ? OR MOUSA ?)/A

     FILE 'WPIX' ENTERED AT 14:10:13 ON 02 FEB 2002
L97       2589 S L19 OR L20 OR L21 OR ASPIRIN?
L98       1436 S 0034/DRN OR R00034/DCN
L99       3158 S L97,L98
L100        61 S L7
                E CELECOXIB/DCN
                E REFECOXIB/DCN
                E COXIB
L101       106 S (CYCLOOXYGENASE OR CYCLO OXYGENASE OR CYCLOOXY GENASE OR CYCL
L102         0 S L15 AND L99
L103        15 S PROSTAGLANDIN?(L)(SYNTHASE OR SYNTHETASE) AND L99
L104        15 S L99 AND L100
L105       126 S L101,L103,L104
L106      1400 S L28
L107         2 S L105 AND L106
L108         6 S L105 AND (ANTIOXID? OR ANTI OXID?)
L109         6 S L107,L108
L110        15 S L100 AND L105
                SEL PN 2
L111         1 S E1-E2 AND L110
L112         1 S L111 AND L97-L111

     FILE 'WPIX' ENTERED AT 14:24:20 ON 02 FEB 2002
```